REMARKS

Applicant respectfully requests reconsideration. Claims 42-74 were previously pending in this application. Claims 44-46, 52-54 and 59-61 are withdrawn. No claims are amended herein. As a result, claims 42-74 are still pending for examination with claims 42, 50, 57, 64 and 68 being independent claims. No new matter has been added.

Rejection Under 35 U.S.C. 112

Applicants thank the Examiner for the indication that the rejection for a lack of written description has been withdrawn.

Claims 42-43, 47-51, 55-58 and 62-74 have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement.

In particular, the Examiner has reviewed the evidence presented by Applicant and concluded that such evidence was not persuasive to overcome the rejection under 35 U.SC. §112 as lacking enablement. In particular, the Examiner has concluded that the "Applicant has not taught or shown the skilled artisan in the art how to harness the immunostimulatory activities to render it therapeutic in the manner relating to the claimed invention." (Office Action page 3). A number of reasons were provided in support of that conclusion, each of which Applicant will address below. However, in general the Examiner is arguing that the art was unpredictable and the data provided in the specification was not sufficient to teach the skilled artisan how to use the claimed invention. Applicant disagrees.

The data provided in the specification identified a new class of compounds, CpG oligonucleotides, for treating disease. It was discovered that oligonucleotides containing an unmethylated CpG dinucleotide were able to mimic the response in a host to bacterial infection. As described in the specification a normal immune response to bacterial infection arises as a result of bacteria breaking apart and releasing DNA into the body. Such DNA is recognized by the immune system and results in the promotion of an immune response that leads to the attack on the invading pathogen. The inventors taught that unmethylated CpG oligonucleotides when administered to a host were recognized by the host as a bacterial infection, causing the induction of an immune

response sufficient to kill an invading pathogen. When CpG oligonucleotides are administered to an infected host the host mounts an immune response to the infection.

The data provided in the specification and discussed in prior responses to Office Action, were sufficient to establish that CpG oligonucleotides were a class of therapeutic agent and that these new therapeutics functioned in a manner similar to bacteria such that they caused induction of a robust immune response in a host capable of treating an infectious disease.

In response to the enablement rejection Applicant submitted publications that were published prior to the invention establishing a nexus between various aspects of the immune response and the treatment of viral infections. The papers were presented for the purpose of establishing what was known by the skilled artisan at the time of the invention. That is, the skilled artisan recognized that induction of certain immune factors was useful for treating viral infection. The skilled artisan would have known and understood that CpG oligonucleotides were useful in the treatment of infectious disease, including papilloma virus. Applicants address below each of the additional points raised by the Examiner in the Office Action.

On page 7 of the office action it is asserted that Poetker et al demonstrate that CpG ODN have failed to demonstrate any therapeutic effect on papilloma growth. Applicants disagree with the characterization of the teachings of Poetker et al. On page 658 Poetker et al teaches that "In preliminary studies, we infected rabbits with papillomas as described and noted papilloma growth in all 4 abdominal infection sites of each infected rabbit at 8 weeks after infection. Starting at 10 weeks after infection we injected 1 of the 4 induced papillomas with 250 μg (50μg/kg) of CpG each week for a total of 3 weeks (3 injections) in 2 separate rabbits and monitored the papilloma size. A decrease in papilloma size was noted within 1 week of the first injection. By the third injection, the treated site had completely resolved, as had the 3 other, remote sites. these observations suggest that CpG therapy is not only capable of inducing a specific inflammatory response that destroys the papilloma, but also capable of inducing a systemic viral immunity that kills distant established papillomas. The rabbits were challenged with a viral load 1 week after the course of CpG injections. That this viral load failed to grow new papillomas after 3 weeks suggest the development of immune memory to the repeat viral challenge." It is clear from this summary that had an important impact on papilloma virus infection in vivo. The authors of the paper then went

on to examine the effect of CpG ODN on rabbits with reestablished papillomas (tumors) and concluded that CpG in the tested model did not have an effect on the papilloma growth. The authors hypothesized that the failure in their model was due to the large tumor burdens in the animals being studied and noted that the CpG ODN administration would have been started earlier had the researchers realized how quickly the tumors grew. (Page 660, column 1). The authors propose that in view of their data that a technique combining tumor removal with CpG demonstration might be effective. While the results in the paper with respect to tumors are interesting, they do not support the finding that CpG ODN are not useful in the treating of papilloma virus infection.

Pages 17-27 of the Office Action are identical to the prior Office Action. Applicant previously addressed each of these arguments in the prior responses to office action. Applicant reiterates those arguments here. However, rather than repeating all of Applicant's arguments, Applicant asks the Examiner to refer to the prior response where each point was addressed.

On Page 4 of the Office Action it is stated that "As provided in the previous Office Actions, it is known in the art that these oligonucleotides induce a TH1 biased immune response, which produces TH1 associated cytokines, and that the induction of a TH1 immune response is also important to resolving infections." As stated in the prior responses, Applicant strongly disagrees with this statement. It was not known in the prior art that these oligonucleotides induce a TH1 biased immune response. This is part of Applicant's invention. Applicant was the first to discover that oligonucleotides containing an unmethylated CpG dinucleotide functioned to produce a robust immune response. It is not possible to consider the enablement of the claimed invention if the Office is improperly considering part of the invention as being part of the prior art. The data provided in the specification related to immune induction, including TH1 cytokines, was data generated in support of the invention.

On page 8 of the Office action it is stated that "It is also noted that Applicant states that the Office is inaccurate when it writes 'At the time the invention, was made, it is well known in the art that the CpG motif present in the oligonucleotide stimulates Th1 immune response…" This statement has been noted, however, contrary to Applicant's assertion, the quoted statement is not provided in the instant nor previous office action." Applicant disagrees. As discussed in the

preceding paragraph, the quoted language is included in the instant office action on page 4. Additionally, it was found on page 11 of the Office Action mailed June 28, 2007.

It is further stated that "However, the same art also recognizes that a balance between a TH1 and TH2 immune response is of importance in resolving infections; see teachings of Infante-Duarte et al." (Office Action page 4). It is believed that the Examiner is referring to Infante-Duarte et al., Springer Seminars in Immunopathology, 1999, 21:317-338. This reference does not form part of the prior art, but rather was published several years after Applicant's priority date.

It is further stated that "Applicant had failed to set forth any guidance as to the type and level of immune profile that the oligonucleotides must ascertain in order to render it therapeutically effective." It is further questioned what level of B cells and NK cells as well as cytokines are necessary to treat papilloma viral infection and it is noted that Krieg et al., Annu. Rev. Immunol., 2002, Vol. 20, 709-760 teaches that oligonucleotides have distinct immune profiles. The skilled artisan reviewing the data and patent application would have expected that oligonucleotides having an unmethylated CpG motif would have the ability to induce an immune response that would be useful in protecting the body against infectious disease. The variability observed with different oligonucleotides containing CG relates to optimization. It would require only routine experimentation for the skilled artisan to identify a CpG oligonucleotide useful in the claimed methods in view of the teaching found in the specification. For instance, the skilled artisan could select an oligonucleotide described in the specification.

Applicants specification provided a teaching of a class of compounds that provided *in vitro* and *in vivo* data establishing the presence of a robust immune response and taught that such an immune response would be useful in the treatment of papilloma viral infections. The skilled artisan at the time of the invention would have recognized that this assertion was true based on the data and what was known in the art at the time of the invention. For instance, Applicant previously cited to the Patent Office Simpson et al, Schneider et al, Morris et al. and Baumgarth et al. describing the correlation between immune factors and treatment of viral infection. Following the invention those of skill in the art, recognizing the utility of this class of therapeutics, based on the disclosure of the instant inventors, and following the guidance provided in the specification, demonstrated as the Applicant had taught that CpG oligonucleotides were useful for treating papilloma viral infection.

The skilled artisan would not need to test numerous parameters to identify an oligonucleotide useful for treating papilloma viral infection. The specification provides a number of species which induce an immune response. The skilled artisan could select from any of these species or, using routine experimentation, could identify other species and test for activity as described in the specification. The routine nature of these selections is evidenced by papers published following the invention which involve the selection of a CpG oligonucleotide and the demonstration that it was useful in treating papilloma viral infections.

On Pages 5-6 of the Office Action Applicant's citation of Simpson et al, Schneider et al, Morris et al. and Baumgarth et al. is addressed. The Examiner states that "none of these references evidence the use of CpG containing oligonucleotides to treat papilloma virus infection. ...none of these references set forth the guidance and direction that the skilled artisan would need to practice the claimed invention. None of these references teach the skilled artisan how to harness the immunostimulatory activity induced by the oligonucleotides to render it therapeutically effective against papilloma virus infection."

Applicants respectfully request that the Examiner reconsider Applicant's arguments with respect to Simpson et al, Schneider et al, Morris et al., and Baumgarth et al. . Applicant did not cite these references to demonstrate that prior to the invention CpG oligonucleotides were useful for treating papilloma virus infections. Rather, these references were cited to establish what was known in the art at the time of the invention regarding a correlation between immune stimulation and the treatment of viral infection. and in particular papilloma viral infection. In Applicant's response Applicant pointed out the data in the specification and indicated that the data demonstrated induction of cytokines which were known in the art at the time of the invention to be correlated with the treatment of viral infection, hence the citation of the references. The refers were not cited to enable the skilled artisan to practice the invention but rather as evidence of what was known in the art at the time of the invention.

Double Patenting Rejection

Claims 42-43, 47-51, 55-58 and 62-74 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 19, of copending Application No. 10/987,146.

US Application No. 10/987,146 has been abandoned. Therefore it is requested that the rejection be withdrawn.

Claims 42-43, 47-51, 55-58 and 62-74 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 42, of copending Application No. 10/382,822.

Applicants elect to defer substantive rebuttal of the rejection on the ground of nonstatutory obviousness-type double patenting as being unpatentable over copending Application No. 10/382,822 until such time as the cited application is allowed.

Claims 42-43, 47-51, 55-58 and 62-74 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 59, of copending Application No. 11/255,100.

Claim 59 of US Application No. 11/255,100 has been withdrawn as being part of a non-elected invention. Claim 59 will be canceled in response to the outstanding office action. Therefore it is requested that the rejection be withdrawn.

Claims 42-43, 47-51, 55-58 and 62-74 have been provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 45, of copending Application No. 11/361,313.

Claim 45 of US Application No. 11/361,313 has been withdrawn as being part of a non-elected invention. Therefore it is requested that the rejection be withdrawn.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, please charge any deficiency to Deposit Account No. 23/2825.

Dated: September 30, 2008

Respectfully submitted,

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